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ORIGINAL ARTICLE

Silica supported sodium hydrogen sulfate and Indion 190 resin: An efficient and heterogeneous catalysts for facile synthesis of bis-(4-hydroxycoumarin-3-yl) methanes

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Abstract 4-Hydroxy coumarin on electrophilic substitution reaction with carbonyl compound in the presence of heterogeneous catalysts ($NaHSO_4 \cdot SiO_2$/Indion 190 resin) offers bis-(4-hydroxycoumarin-3-yl) methanes in good to excellent yields.

1. Introduction

Heterocyclic compounds with oxygen containing moieties are industrially very important as they serve as precursors. Coumarins, found naturally in various plants are the members of a class of heterocyclic compounds (Hinman et al., 1956). They are extensively employed as food and cosmetic additives (Okenne and Thomes, 1997), also in dye lasers as gain and stabilizing media (Zahradnik, 1992). Their identity as biologically active compounds, after the discoveries of them being anticoagulant, antibiotic, antitumor, anti-HIV, antihypertensive, analgesic, anti-inflammatory and anti-arrhythmia agents have made them highly sought after precursor molecules in pharmaceutical industries (Stahmann et al., 1947; Murray et al., 1982; Chen et al., 1999).

This crucially important coumarin faces numerous shortcomings during its synthesis rising through the use of tedious methodologies those that require organic solvents, labor and cost consuming workup procedures, long reaction times which generally end up with low product yields. Improvements in these conditions required the development of efficient, cost effective, safe, mild and environmentally benign procedures for coumarin

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synthesis. Over the years the concept of green chemistry is making researchers discover and develop various new strategies. In the same context a number of methods have so far been reported for the synthesis of biscoumarin (Manolov et al., 2006; Kadir et al., 2008; Kidwai et al., 2007; Mehrabi and Abusaidi, 2010). Heterogeneous catalysts have gained much importance in recent years due to economic and environmental considerations (Ramesh et al., 2003; Banerjee et al., 2004; Das, 2004). These catalysts are generally less expensive, highly reactive, eco-friendly and convenient to handle as well as eliminate the use of volatile and toxic organic solvents.

Thus, considering the above reports, advantage and applications of silica-supported sodium hydrogen sulfate/Indion 190 resin as a heterogeneous catalyst and as part of our efforts to develop the green methodologies for organic transformations (Chaskar et al., 2009a,b, 2011; Phatangare et al., 2009; Gawand et al., 2009; Takale et al., 2011), we hereby report the effective and practical one-pot synthesis of biscoumarinyl methane derivatives by two-component one-pot domino Knoevenagel-type condensation/Michael reaction between 4-hydroxycoumarin and aromatic aldehydes in the presence of a catalytic amount of silica-supported sodium hydrogen sulfate or Indion 190 resin as a heterogeneous catalyst (Scheme 1). Indion 190 resin is commercially available while $NaHSO_4{\cdot}SiO_2$ can be easily prepared (Breton, 1997) from the readily available inexpensive ingredients, $NaHSO_4$ and silica gel (finer than 200 mesh) and it should be properly activated.

2. Result and discussion

In order to investigate the catalyst efficiency for the condensation of 4-hydroxycoumarin and benzaldehyde, different catalysts were screened and $NaHSO_4{\cdot}SiO_2$ and Indion 190 resin were found to be the best catalysts for the synthesis of bis-(4-hydroxycoumarin-3-yl) methanes derivative (Table 1).

In order to elucidate the role of the $NaHSO_4{\cdot}SiO_2$/Indion 190 resin as catalyst, a control reaction was set up using 4-hydroxycoumarin (2 mmol) and benzaldehyde (1 mmol) in toluene in the absence of a catalyst. The control reaction ended up with the formation of 19% of biscoumarinyl methane. However the test reaction set up with the same substrate, using 150 mg of $NaHSO_4{\cdot}SiO_2$/Indion 190 resin at 100 °C in toluene afforded the products in quantitative yield in 30 min. It is postulated that the $NaHSO_4{\cdot}SiO_2$/Indion 190 resin plays a complex role in accelerating the coupling reaction and thus promotes the formation of products. The methylidene-2*H*-chromene-2,4(3*H*)-dione intermediate is formed by the nucleophilic addition of 4-hydroxycoumarin to aldehydes in the presence of $NaHSO_4{\cdot}SiO_2$/Indion 190 resin. Michael addition of methylidene-2*H*-chromene-2,4(3*H*)-dione with second mole of 4-hydroxycoumarin followed by dehydration afforded the corresponding products (Scheme 2).

Table 1 Optimization of the catalyst for the synthesis of bis-(4-hydroxycoumarin-3-yl) methanes.[a]

Entry	Catalyst	Time	Yield[b] (%)
1	Phosphotungstic acid	45 min	73
2	Phosphomolybdic acid	1 h	66
3	Phosphoric acid	1 h	62
4	Sulfuric acid	1 h	61
5	TBAB	1 h	80
6	Silicotungstic acid	1 h	68
7	–	24 h	19
8	*p*-TSA	02 h	50
9	$NaHSO_4{\cdot}SiO_2$	30 min	89
10	Indion 190 resin	30 min	92

[a] Reagents and reaction conditions: 4-Hydroxycoumarin (2 mmol), benzaldehyde (1 mmol), catalyst (150 mg), 100 °C, toluene (5 mL), time 30 min.
[b] Isolated yield.

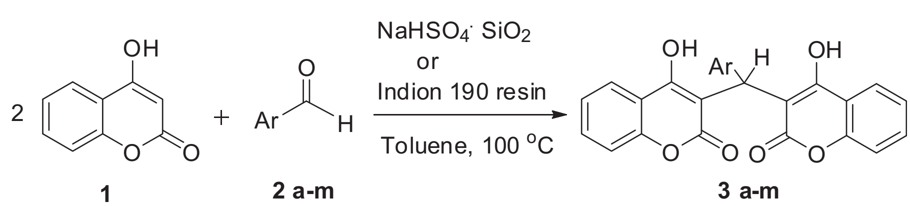
We observed that catalyst concentration also plays a vital role in the synthesis of bis-(4-hydroxycoumarin-3-yl) methanes. After varying the concentration of $NaHSO_4{\cdot}SiO_2$, we got optimum yield with 150 mg of catalyst (Table 2). On further increasing the amount of catalyst, the yield of corresponding product decreased, ascribable to increased acidity.

To investigate the feasibility of this synthetic methodology for the synthesis of bis-(4-hydroxycoumarin-3-yl) methane derivatives, we extended the reaction of 4-hydroxycoumarin with a range of aromatic aldehydes under similar conditions, furnishing the respective bis-(4-hydroxycoumarin-3-yl) methanes derivatives in high yields. The optimized results are summarized in Table 3. The method has the ability to tolerate a variety of functional groups such as bromo, chloro, nitro and methoxy. The products synthesized thus were obtained in good to excellent yields and characterized by ^{1}H NMR, ^{13}C NMR and physical constant. Physical and spectral data of known compounds are in agreement with those reported in the literature (Kidwai et al., 2007; Khurana and Kumar, 2009; Singh et al., 2010).

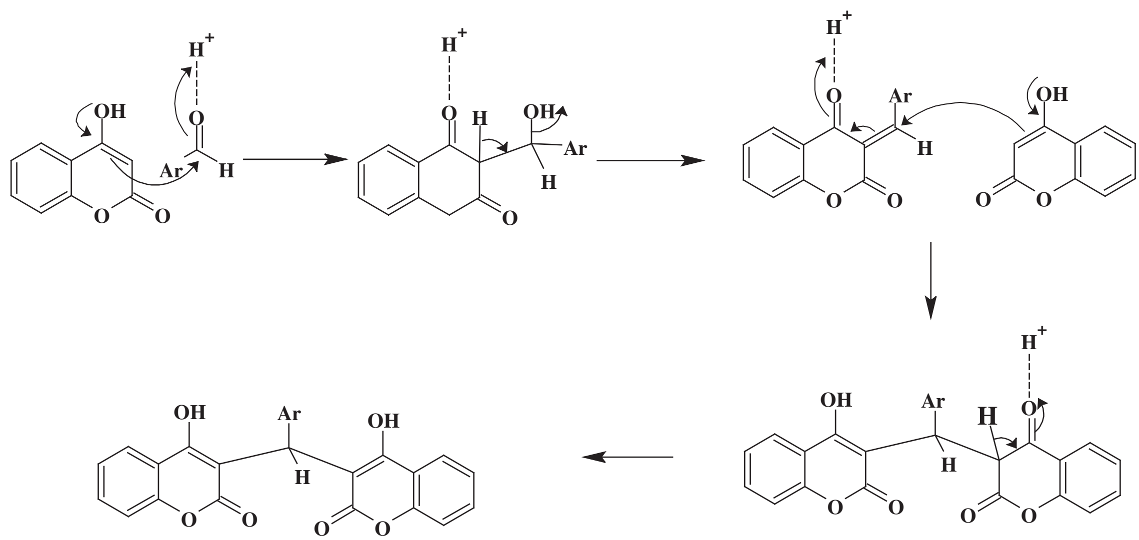
With the increasing interest in human health and environmental protection, more attention is being paid to green chemistry. With this view we studied the recyclability and reusability of the catalyst. After completion of the reaction the catalyst was separated by filtration, washed with hexane and dried. The activated catalyst was used for two more subsequent cycles. To our surprise consistent performance of the catalyst is observed in all the cycles Table 4.

3. Experimental

All commercial reagents were used as received without purification and all solvents were of reagent grade. The reaction



Scheme 1 Synthesis of biscoumarin derivatives.



Scheme 2 Proposed mechanism for the synthesis of bis-(4-hydroxycoumarin-3-yl) methanes.

Table 2 Optimization of the amount of $NaHSO_4{\cdot}SiO_2$/Indion 190 resin for the synthesis of bis-(4-hydroxycoumarin-3-yl) methanes.[a]

Entry	Wt. of catalyst (mg)	Yield[b] (%)	
		$NaHSO_4{\cdot}SiO_2$	Indion 190 resin
1	50	40	40
2	100	60	58
3	150	89	92
4	200	83	85
5	250	75	80

[a] Reagents and reaction conditions: 4-Hydroxycoumarin (2 mmol), benzaldehyde (1 mmol), catalyst (X mg), 100 °C, toluene (5 mL), time 30 min.
[b] Isolated yield.

was monitored by TLC using 0.25 mm E-Merck silica gel 60 F254 precoated plates, which were visualized with UV light. Melting points were taken in open capillaries. The IR spectra were recorded on a PerkinElmer 257 spectrometer using KBr discs. ^{1}H NMR and ^{13}C NMR spectra were recorded on a VXR-300 MHz instrument using TMS as the internal standard.

3.1. General experimental procedure

To a mixture of a 4-hydroxycoumarin (2 mmol), aldehydes (1 mmol) in toluene (5 ml) $NaHSO_4{\cdot}SiO_2$/Indion 190 resin (150 mg) was added. The mixture was stirred at 100 °C for 30 min, after completion of the reaction, as indicated by TLC, the reaction mixture was filtered. The catalyst was recovered from the residue and the filtrate was concentrated under reduced pressure to isolate the product. The crude product was crystallized by using IPA to afford the pure product.

Table 3 Synthesis of bis-(4-hydroxycoumarin-3-yl) methanes.[a]

Entry	Reactant	Ar	Product	Yield[b](%)		M.P. (°C)/(lit.)
				$NaHSO_4{\cdot}SiO_2$	Indion 190 resin	
1	**2a**	C_6H_5	**3a**	89	92	229 (228–230)
2	**2b**	4-ClC_6H_4	**3b**	90	91	251 (252–254)
3	**2c**	4-BrC_6H_4	**3c**	88	91	266 (266–268)
4	**2d**	$4\text{-NO}_2C_6H_4$	**3d**	91	93	233 (232–234)
5	**2e**	$4\text{-CH}_3C_6H_4$	**3e**	90	90	269 (266–268)
6	**2f**	4-OHC_6H_4	**3f**	86	89	223 (222–224)
7	**2g**	$4\text{-CH}_3OC_6H_4$	**3g**	89	91	244 (242–244)
8	**2h**	2-ClC_6H_6	**3h**	87	87	224 (224–226)
9	**2i**	2-BrC_6H_4	**3i**	87	89	258
10	**2j**	2-OH C_6H_4	**3j**	85	87	254 (254–256)
11	**2k**	$3\text{-NO}_2\ C_6H_4$	**3k**	90	90	235 (234–236)
12	**2l**	4-*N*,*N*-Dimethyl C_6H_4	**3l**	88	91	221 (222–224)
13	**2m**	4-*N*,*N*-Diethyl C_6H_4	**3m**	87	90	236

[a] Reagents and reaction conditions: 4-Hydroxycoumarin (2 mmol), aldehydes (1 mmol), $NaHSO_4{\cdot}SiO_2$/Indion 190 resin (150 mg), toluene (5 mL), temperature: 100 °C, time: 30 min.
[b] Yield: isolated.

Table 4 Reusability of the catalyst.[a]

Cycle	Yield[b] (%)	
	$NaHSO_4 \cdot SiO_2$	Indion 190 Resin
1	89	92
2	86	90
3	80	87

[a] Reagents and reaction conditions: 4-Hydroxycoumarin (2 mmol), benzaldehyde (1 mmol), $NaHSO_4 \cdot SiO_2$/Indion 190 resin (150 mg), 100 °C, toluene (5 mL), time 30 min.
[b] Isolated yield.

3.2. Representative spectral data

Compound **3a**:
^{1}H NMR: (DMSO-d_6): δ 6.20 (s, 1H), 6.90–7.50 (m, 13H).
^{13}C NMR: (DMSO-d_6): δ 16.0, 91.0, 105.2, 108.1, 116.0, 117.3, 124.0, 125.4, 126.1, 127.0, 128.7, 130.0, 132.5, 140.0, 163.1, 166.3.
IR (KBr): 3032, 1655, 1609, 754.
Mp: 229 °C (Lit. 228–230 °C);
Compound **3b:**
^{1}H NMR: (DMSO-d_6): δ 6.18(s,1H), 7.10–7.80 (m, 12H).
^{13}C NMR: (DMSO-d_6): δ 16.0, 91.0, 105.1, 107.3, 115.0, 118.2, 124.4, 125.2, 126.0, 127.2, 129.1, 130.0, 133.4, 139.5, 163.0, 166.1.
IR (KBr): 3032, 1663, 1609, 759.
Mp: 251 °C (Lit. 252–254 °C).

4. Conclusion

In summary, we have developed a novel, simple and efficient protocol for the synthesis of bis-(4-hydroxycoumarin-3-yl) methane derivatives via two-component one-pot domino Knoevenagel-type condensation/Michael reaction between 4-hydroxycoumarin and aromatic aldehydes in the presence of a catalytic amount of silica-supported sodium hydrogen sulfate or Indion 190 resin as a heterogeneous catalyst. The method is associated with the several benefits derived from multicomponent reaction and the application of a heterogeneous catalyst. We feel this eco-friendly and economically viable catalyst will find practical utility for the one-pot synthesis of bis-(4-hydroxycoumarin-3-yl) methane derivatives.

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